Gout Education Society

Medical Professional Guide:

Gout Diagnosis and Treatment

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A letter from the

Chairman of the Gout Education Society

On behalf of the Board of Directors of the Gout Education Society, I'm pleased to offer this Medical Professional Guide on gout diagnosis and treatment. It was created to provide the latest perspective and information for all front-line medical professionals who see potential gout sufferers and new gout patients.

Gout incidence is on the rise. This extremely painful, inflammatory arthritis now affects more than 9.2 million Americans—about 4% of the adult population. Some of the rise can be associated with increased patients with obesity, high blood pressure, insulin resistance and blood lipid issues. Our research tells us, however, that two out of three gout patients aren't happy with how their physician is treating their gout—and only 10% of gout sufferers are getting the guideline-recommended treatment they need. This happens for a multitude of reasons—including sufferers relying on home remedies, patient non-adherence with treatment and misdiagnosis.

As rheumatology specialists who specifically treat gout, our Board's goal is to raise awareness about the growing patient numbers, and to make sure more sufferers receive a proper diagnosis and ongoing, necessary treatment—combining a healthy diet and exercise with the right medication. Through our "Kick Gout in the Acid" campaign, we are encouraging those with gout to get their uric acid levels checked every six months and aim for a healthy level of 6.0 mg/dL or below.

Our Board believes this guide can be a helpful tool, because many medical professionals—including PCPs, ER physicians, nurse practitioners, podiatrists, and orthopedic surgeons—treat varying numbers of gout patients, and therefore have varying levels of exposure to the disease. Our hope is this information will offer evidence-driven counsel on consistent disease diagnosis and treatment, which will result in better care and more optimal outcomes.

If we can provide specific assistance to you, or answer questions, please reach out to us at: **GoutEducation.org**.

We're here to help reduce the overall burden of gout and encourage more patients to "Kick Gout in the Acid." We hope you will join this national effort to improve the lives of gout sufferers.

Sincerely,

N. Lawrence Edwards, MD, MACP, MACR
Gout Education Society Chairman and CEO

By the Numbers:

The Need for Patient Education

Only **1 in 3** gout patients gets their uric acid levels checked every six months.

Half of those with gout do not recognize the classic symptoms of gout, including swelling of a joint and sudden, severe pain.

1 in 5 sufferers says *nothing* is more painful than a gout flare.

Surveys conducted in the United States by Wakefield Research on behalf of the Gout Education Society suggest that today's population has little knowledge of gout—a disease shrouded in myths, ambiguity, misconceptions and stigmas. Consider that:

- **Nearly two-thirds of gout sufferers do not know gout is a form of arthritis.**
- **Only 1 in 3 gout patients gets uric acid levels checked every six months.**
- **Only 1 in 3 gout patients takes daily medications as prescribed to lower uric acid levels—and two-thirds incorrectly think that drinking cherry juice is just as effective in treating gout than taking medications.**
- **4 in 10 gout patients say their quality of life is not as good because of gout.**
- **Nearly 9 in 10 gout sufferers agree it is a serious health issue that requires ongoing treatment and management, but only 1 in 3 takes daily medications, as prescribed, to lower uric acid levels.**
- **Few Americans understand the connection between gout and other serious health issues**
- **Only 4 in 10 know that obesity is a risk factor.**
- **Just 3 in 10 know that diabetes is a risk factor.**
- **Only 1 in 4 knows kidney disease is a risk factor.**
- **Just 3 in 10 know that high blood pressure is a risk factor.**

Findings from the surveys also confirm that, in addition to the physical pain of gout, the disease also presents a tremendous emotional burden to those who have it. Yet, due to the myths and stigma associated with gout, most gout sufferers do not take the appropriate steps to keep flares under control. Less than half of people with gout say treating their gout is a priority, reaffirming the need for consistent patient education on the part of medical professionals who are responsible for their care.

- **9 out of 10 people with gout worry about it.**
- **1 in 5 with gout says nothing is more painful than a gout flare.**
- **1 in 4 with gout says gout controls his or her life.**
- **1 in 4 frequently misses work because of gout.**
- **More than half of people with gout are embarrassed to have it.**

Steps Toward Correct Diagnosis

Diagnosing Gout

Gouty arthritis is one of an estimated 107 types of arthritis and is the most common form of inflammatory arthritis. Rheumatoid arthritis and psoriatic arthritis are also in the inflammatory arthritis category, but incidence is far less than that of gout. Aspiration of synovial fluid from an actively inflamed joint and identification of monosodium urate crystals through a polarizing microscope is the gold standard for making a correct diagnosis of gout.

As technology continues to advance, many clinicians also believe that MRIs and ultrasounds can detect the presence of tophi in all stages of gout, helping to identify the disease earlier and less invasively.

While aspiration of synovial fluid is the gold standard for diagnosing gout, physicians and other healthcare providers rarely make a diagnosis this way, given the need for specialized equipment and training. Therefore, most physicians must make a probable diagnosis based on how closely symptoms align with the classic description of symptoms.

Typical clinical features associated with gout, which the American College of Rheumatology (ACR) Guideline for the Management of Gout consider a good clinical diagnosis, include the following:

Sudden, Severe Pain

A classic sign of gout is the sudden onset of excruciating pain that escalates rapidly from a joint that otherwise has no symptoms to one that is severe, very swollen, red and inflamed over a 12-hour period. The pain stays at that level for several days and gradually wanes over a period of 5 to 7 days. For patients who have experienced several of these episodes followed by an asymptomatic period, this is highly suggestive of gout.

Hyperuricemia: Can Lead to Gout

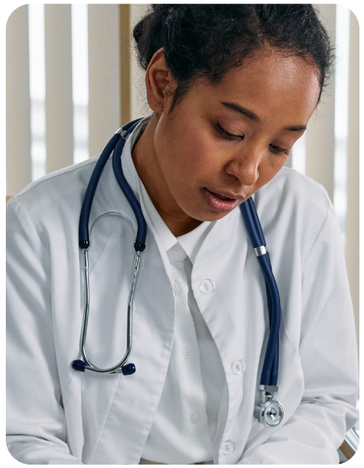
Another clinical feature for gout is hyperuricemia, a common biochemical abnormality. At least 20% of the population has an elevated uric acid (UA) level, which is defined as above 7.0 mg/dL. This is the level at which UA could potentially come out of solution and form problematic crystals. Although it is the metabolic underpinning of gout, UA is often not elevated during an acute flare. UA levels while a patient is in significant pain can be lowered by 2.0-2.5 mg/dL from the baseline reading. This is a common cause of misdiagnosis, or a missed diagnosis. Furthermore, hyperuricemia alone does not make for a diagnosis. Most people with hyperuricemia do not ever develop gout, although the higher the uric acid level, the more likely someone is to develop it.

Studies have shown:

- Only an estimated **1 in 5** people with UA above 7.0 mg/dL will ever experience symptoms of gout.
- Those whose UA level is above 9.0 mg/dL have a **1 in 2** chance of developing gout.

Distinguishing Gout from Other Conditions

Gout may be confused with infectious arthritis, which is also called septic arthritis and is a severe condition. Like gout, it can cause rapid, very painful inflammation.



Infectious arthritis can result from pneumonia, an abscess or a post-surgical infection elsewhere in the body. Drawing fluid from the joint and checking it for bacteria is important in these cases.

Another disease process that mimics and can be confused with gout is pseudogout. Clinically, it looks much like gout but is caused by calcium pyrophosphate crystals. Typically, it presents with milder swelling and pain but can be more severe and closely imitate gout. Pseudogout is usually found among people ages 65 and older. Osteoarthritis, the most common non-inflammatory arthritis, is one of its risk factors.

Considering Family History

Another consideration is the genetic component. Anyone with a family history of gout may be at greater risk, although there is much more to learn about the role genetics play in the disease. Some known genetically inherited problems such as certain enzyme abnormalities and abnormalities in how kidneys transport and eliminate UA can play a role in high UA levels.

Gout is a disease of "clusters" in families; those with a parent who had gout are more likely than the general population to get the disease. It is important to note that lifestyle issues, such as obesity and a diet rich in gout unfriendly foods, are risk factors often shared by family members. As with many lifestyle issues, some of these factors are modifiable and others are not.

What to Ask Patients

Review and confirm the patient's health history. For patients with a number of comorbid medical conditions, such as heart disease, hypertension, hyperlipidemia, type 2 diabetes, obesity, metabolic syndrome, liver disease or chronic kidney disease, there is a greater suspicion that the joint symptoms may be gout.

Review the course of the pain during the flare. Typically, there are intermittent episodes of severe pain, with no pain experienced in between the episodes. As flares continue over the years, painful episodes will increasingly last longer.

Ask the following questions to help in making an assessment:

1. Have you had any previous episodes that resemble the symptoms you are experiencing today?
2. Are there any events that may have triggered the symptoms, e.g., excessive consumption of alcohol or foods/beverages with high levels of purine or high fructose corn syrup?
3. Have you experienced any trauma to the inflamed joint?
4. Have there been any changes to the medications you take for other health conditions?
5. Have there been any changes to your diet or exercise routine?
6. Is there a family history of gout?

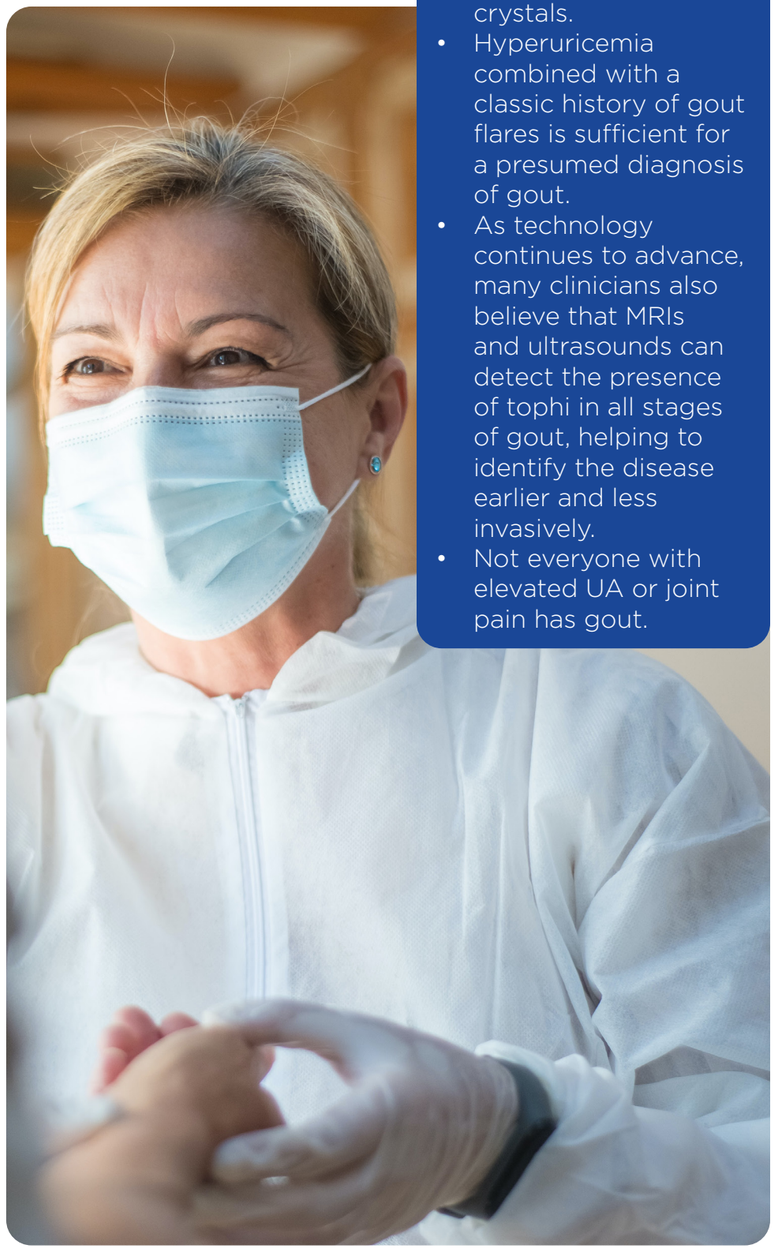
The bottom line for most primary care physicians in making a diagnosis is whether the patient has presented symptoms in typical fashion and if their UA is elevated during a time when they do not have severe symptoms.

Once these are confirmed, a presumptive diagnosis can be made and treatment should begin. The more distant or atypical the case, the less assurance there is that gout is present. In such cases, referral to a rheumatologist to confirm the diagnosis may be appropriate.

Cautions

Medical professionals should be meticulous in making a diagnosis of gout unless they have witnessed symptoms firsthand and flares follow a classic history. Not everyone with elevated UA and joint pain has gout. There must be extensive evidence of inflammation not caused by infection, and the pain must be very severe. In men, the pain is usually in the lower extremities initially. Women usually experience initial pain in the upper extremity joints.

The diagnosis of gout is assured if the synovial fluid examination reveals monosodium urate crystal or if tophi are clinically evident or if classic gouty erosions are present on radiographer. A “presumed diagnosis” is made if the patient describes multiple, recurrent episodes of rapid-onset severe joint pain with resolution over 5-10 days who is hypouricemic between flares. The physician should always have infectious arthritis in their differential diagnosis.



- A definitive diagnosis of gout requires aspiration of synovial fluid and the presence of monosodium crystals.
- Hyperuricemia combined with a classic history of gout flares is sufficient for a presumed diagnosis of gout.
- As technology continues to advance, many clinicians also believe that MRIs and ultrasounds can detect the presence of tophi in all stages of gout, helping to identify the disease earlier and less invasively.
- Not everyone with elevated UA or joint pain has gout.

The Demographics of Gout

Caucasian and African American Men

Gout flares typically occur in men in their 40s or 50s and usually after years or decades of high UA levels. Gout is more common in men because they attain their adult UA level at puberty while women are protected by the uricosuric effects of estrogen through their early adult life. Because of this, men can start accumulating extra UA in the form of crystals decades before women. While the incidence of gout in both elderly men and women eventually reaches some parity, the overall prevalence of gout skews male because men reach their adult UA level much sooner.

Multicultural Patients

Gout is a worldwide disease and is increasing in prevalence. The same types of factors leading to increasing incidence in the U.S., such as the obesity epidemic, are responsible for increasing incidence and prevalence of the disease elsewhere in the world. Since gout is also a disease of uric acid accrual, increased longevity in both developed and undeveloped countries means that the incidence will continue to rise.

Heredity and genetics are the most important determinants of how common gout is in a country. The highest prevalence is seen in the Maori of New Zealand and the aborigines of Taiwan with estimates of >10%. In North America and Western Europe the disease is common at between 1-4%. Gout is much less common in Central and South America, Africa and most of Asia.

In ethnic populations where the prevalence of gout is high, the disease tends to have a more accelerated course with a more rapid progression to tophus development and destructive arthritis. This is due to more marked elevations of UA levels.

Post-menopausal Women and Gout

Women are at their greatest risk of gout in their post-menopausal years. At the same time, the risk for any particular woman is low. From a young age through their child-bearing years, women’s UA levels remain at the low 3.0-6.0 mg/dL range established in childhood. Once they start to experience the gradual loss of estrogen over the next three decades, there is a gradual increase in their serum UA levels. Post-menopause, some women are at risk for gout if their UA rises above 7.0 mg/dL. Typically these are women with a family history of gout, have some form of chronic kidney disease or are taking medications that raise UA, such as hydrochlorothiazide. Women at risk may not experience symptoms for a decade following menopause unless they have another metabolic or medical problem. For those with a family history or other risk factors, or those taking a drug that can raise UA levels, testing their UA level is prudent.

- Be cautious of the stereotype that gout only afflicts overindulgent men.
- While gout is more prevalent in men, the decrease in estrogen in post- menopausal women can put them at risk.
- Gout can affect anyone at any time—so everyone should be aware of the risk factors and symptoms. Gout is as serious as rheumatoid arthritis and requires lifelong care once diagnosed.
- Gout has a similar disease process across all ethnic groups, although it is more prevalent and more aggressive in some populations.
- Certain ethnic populations have a higher risk for comorbid conditions that can impact the development and progression of gout.

Gout Flares and Long-term Joint Impact

The ACR Guideline for the Management of Gout confirms that therapy to lower UA is appropriate for patients who fit into one of several categories:

1. Any patient with a history of 2 or more flares, the presence of 1 or more tophi or evidence of radiographic damage attributable to gout.

2. Any patient with a single flare and moderate-severe chronic kidney disease or urolithiasis.

Location of Gout

For some patients, gout always stays in one of the big toes. But, as a general rule, gouty arthritis moves around. For example, if the first affected joint is the right toe, the condition might move on to the left ankle, then to the mid foot of the left foot. In men, gout may initially skip between the lower extremities and stay there for years before moving on to upper extremity joints such as the wrist, elbow or small joints of the fingers. The more repeat flares a patient has in the early stage of gout, the more likely gout will affect several joints simultaneously. As time progresses, and the patient is not placed on urate-lowering therapy, the frequency and duration of flares along with the number of joints affected will increase.

While women can present with similar symptoms as men (e.g., pain and inflammation in the great toe and intermittent flares), symptoms usually follow a different pattern. Women are more likely to experience early symptoms in the upper extremities such as the wrist, small finger joints and elbow. Nodal (lumpy) osteoarthritis is a common form of hand arthritis in older women. Sudden pain in the nodules could signal that there is gout in the joint. Women may also experience symptoms in other joints.

Onset and Progression of Gout Flares

Early on, flares occur with a relatively short duration of five to seven days. After a first flare, it can be difficult to predict when the next one will strike—anytime from several months (11 is average) to several years later. Most patients will experience two flares during their first year of symptoms; this is an important trigger that it is time to start a UA-lowering therapy.

Because flares may occur infrequently in the beginning, gout patients often go untreated or may only experience one flare per year. The prevalence of gout flares will grow more frequent, however. For example, the frequency of flares might increase from every 11-12 months initially to every 6-8 weeks after a decade without proper treatment. Similarly, the duration of each flare may increase from 5-7 days to 2-3 weeks during this same decade.

The bottom line: the frequency and duration of flares will increase over time if a patient is not put on UA-lowering therapy.

Typically High Pain Level

The pain experienced during a gout flare is usually quite intense—rated an average of 8.5 on a 10-point scale. It usually leaves the patient unwilling to even move the affected joint. If the foot or knee are involved, weight-bearing will seem impossible.

As the Disease Advances: Continuous Joint Symptoms and Subcutaneous Tophi

Subcutaneous tophi are a mass of monosodium urate crystals that develops in fibrous tissue around the joints as a result of hyperuricemia. With the help of modern MRIs and ultrasounds, clinicians now believe that all stages of gout involve tophi. Even in early-stage gout, or before a patient develops symptoms, UA crystals begin depositing in and around the joint. This is characterized by a thin layer of crystals across the cartilage in the joint or small nodules of crystals deposited inside the joint. The nodules grow over time to be felt on physical examination and can become large and disfiguring. In some patients, they will erupt to the surface and drain the chalky uric acid crystals.

The higher the UA level, the more rapidly the UA deposits will accumulate around the joints. A typical male patient who develops gout at age 50 and is inadequately treated with uric acid- lowering medication will go through a decade or slightly more (10-12 years) experiencing these acute and intermittent flares. They will become more frequent and last longer, albeit with asymptomatic joints between flares. After approximately a decade without appropriate treatment, the patient might enter into a stage of advanced gout in which symptoms are present consistently—either as flares or chronic aching and pain in the joint.

A more aggressive form of gout will develop in patients who take drugs like cyclosporine or tacrolimus following organ transplantation of the heart, kidney or liver. In such cases, the time frame of elevated UA leading to gout symptoms and tophi may be significantly shorter. Tophi may begin to manifest within several years of beginning these drug regimens.

Complete Therapy for Gout

Before Choosing a Course of Treatment

There are a number of comorbid diseases associated with gout, such as heart disease, kidney disease, liver disease, obesity, hypertension and diabetes. Once a gout diagnosis is made, it is important to consider these comorbid diseases and how commonly used UA-lowering therapies may impact the patient's overall health. For example, avoid prescribing non-steroidal anti-inflammatory drugs (NSAIDs) for patients with kidney or heart disease and corticosteroids for patients with severe diabetes.

Physicians also need to be cognizant of what anti-inflammatory therapies patients can tolerate. For example, a patient who experienced gastrointestinal problems while on colchicine should not receive it as treatment again. Always ask the simple question, "What have you taken before and what was effective?"

Recommended Drug Therapy for Gout Flares

The treatment of gout has two major goals:

1. Elimination of pain of an acute flare and resolution of the flare.
2. Prevention of disease progression by lowering the serum uric acid level to less than 6.0 mg/dL which, over time, prevents acute flares, increases the resorption of tophi and decreases and/or slows down the progression of joint destruction.

The treatment focus for patients experiencing gout flares typically begins by eliminating the pain as quickly as possible. For acute gout flares, the standard therapies include: colchicine, NSAIDs, some form of corticosteroid like prednisone or Medrol, or injections of corticosteroids such as triamcinolone or Depo-Medrol. Some patients will simply tolerate one form better than others. Most primary care physicians use NSAIDs such as naproxen (Naprosyn®, Aleve®), ibuprofen (Advil®) or indomethacin (Indocin®), but most NSAIDs would be equally effective.

High-dose ibuprofen at 800 mg three times per day for several days, followed by 600 mg, three times per day for another week, is appropriate. Naproxen can be given at 500 mg, two times per day and then cut down to 375 mg after several days, for a total of 10 days. See the chart for more specific recommendations.

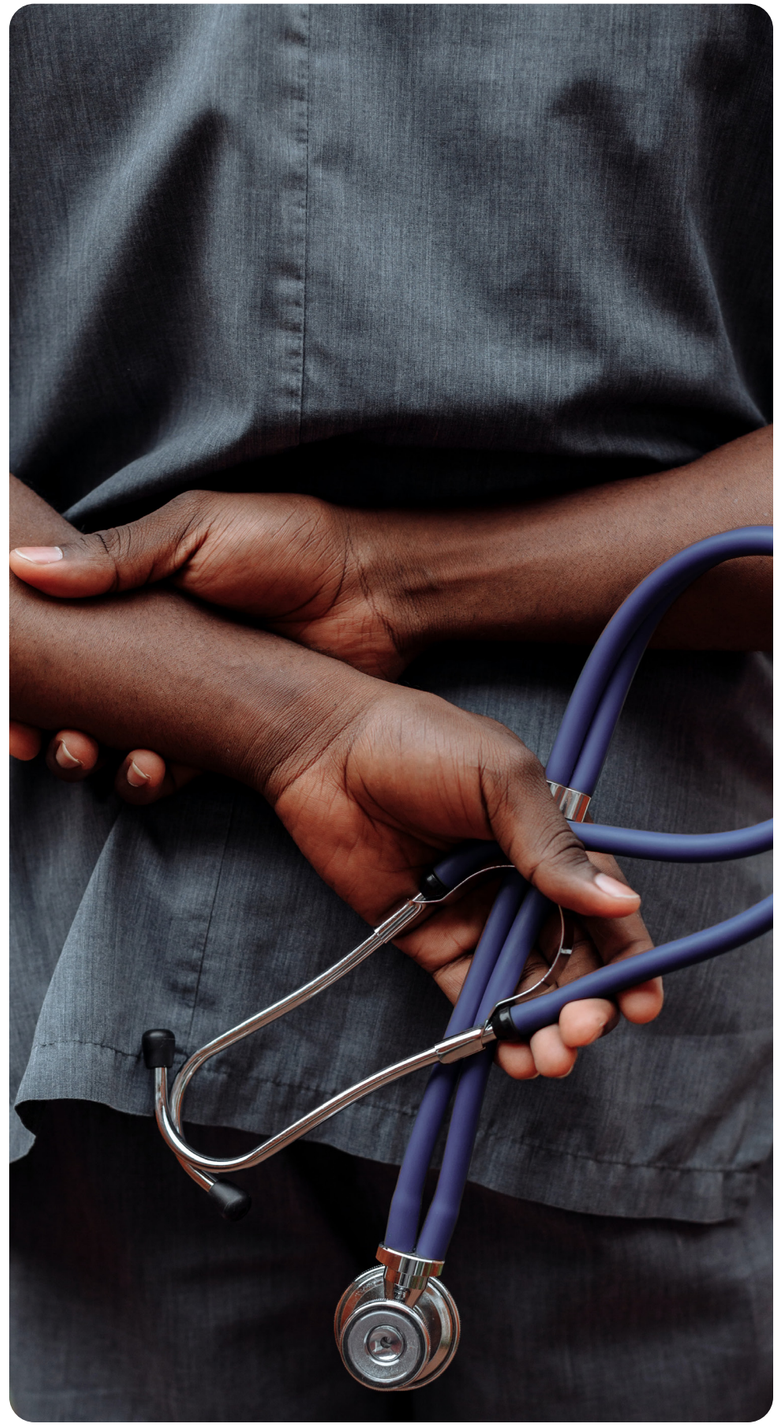
The other options for treating flares are colchicine and corticosteroids. The "low- dose" colchicine regimen of two tablets (1.2 mg) as early in the flare as possible, followed by another tablet (0.6 mg) an hour later and then continue with a tablet once or twice daily over the next week is an effective approach. Corticosteroids in the form of prednisone or medrol may be given orally as a tapering dose from 40 mg/day to completely off over a 7-10 day period. The most important thing about treating with any of these anti- inflammatory therapies is that the earlier the medication is initiated, the more effective it will be.

While all of these options provide short-term relief and help reduce inflammation, they are a temporary solution. Flares will return until the underlying problem (elevated UA) is addressed. UA-lowering therapy is the cornerstone of preventing gout progression over time.

NSAIDs and the Food and Drug Administration

Over the past decade, the Food and Drug Administration (FDA) has monitored and evaluated the safety of NSAIDs. In 2005, the FDA began requiring manufacturers to include new safety warnings on prescription NSAID labels. Recently, the FDA strengthened its warning about NSAID use to emphasize that patients taking NSAIDs are at greater risk for heart attack or stroke.

Talk to your patients before you prescribe an NSAID for the treatment of gout. Be careful to explain to them that taking a higher dose than recommended might lead to other long-term health problems.



Therapies to Relieve Pain and Reduce Swelling of Acute Gout

Name	Dosage	Special Instructions	Possible Side Effects	Be Aware
Colchicine Colcrys®, Mitigare®	Two tablets (1.2 mg) immediately then one tablet (0.6 mg) after one hour. Then one tablet once or twice daily for a week.	Take with food if stomach upset occurs. Drink plenty of fluids.	Diarrhea; nausea or vomiting; stomach pain.	High dose colchicine for acute flares is inappropriate. Colchicine should be used with caution in people with renal disease, those with bone marrow suppression and should not be used in those on clarithromycin or erythromycin.
Glucocorticosteroids Medrol®, Deltasone® and Kenalog®-40	Kenalog 60 mg x1, followed by low dose steroids or oral prednisone given at 30 mg with a taper to 0 mg over 10 days		Retention of sodium (salt) and fluids; weight gain; high blood pressure; loss of potassium; poor glucose control; and headache.	Particularly useful for those with chronic kidney disease. Use with caution in diabetic patients.
Non-steroidal anti-inflammatory drugs (NSAIDs) Celecoxib (Celebrex®); Ibuprofen (Advil®, Motrin®); Indomethacin (Indocin®); Naproxen (Aleve®, Naprosyn®)	High dose of any non-steroidals given for first 3 days, followed by moderate doses for an additional 7 days.		Nausea; stomach discomfort; retention of sodium; and fluids; dyspepsia; gastric ulcers; and headache.	May interact with blood pressure and heart medications, especially in the elderly. Use caution in patients with a history of GI ulcers, kidney disease and the elderly.

Anti-Inflammatory Prophylaxis for Prevention of Gout Flares

Name	Dosage	Special Instructions	Possible Side Effects	Be Aware
Colchicine Colcrys®, Mitigare®	Take one tablet (0.6 mg) once or twice daily. Patients with severe kidney disease may only need one tablet every other day or every third day, depending on creatinine clearance.	Take with food if stomach upset occurs. Drink plenty of fluids.	Diarrhea; nausea or vomiting; stomach pain.	Some people are very sensitive to colchicine. If diarrhea or abdominal pains occur, dosage should be reduced. There are many drug-drug interconnections with colchicine.
Non-steroidal anti-inflammatory drugs (NSAIDs) Celecoxib (Celebrex®); Ibuprofen (Advil®, Motrin®); Indomethacin (Indocin®); Naproxen (Aleve®, Naprosyn®)	Low dose of any non-steroidals may be used prophylactically for the first six months of urate-lowering therapy.		Nausea; stomach discomfort; retention of sodium; and fluids; dyspepsia; gastric ulcers; and headache.	May interact with blood pressure and heart medications, especially in the elderly. Use caution in patients with a history of GI ulcers, kidney disease and the elderly. Ulcers may occur without any preceding symptoms.

Long-term UA Management

Most people who develop gout need life-long therapy. It will take time to determine the correct UA-lowering therapy dosage that will enable a patient to reach and maintain the target range. Generally, once the target is reached the patient stays on that dosage year-after-year. However, it may be necessary to increase or decrease the dosage if a patient adds or changes other medications that could alter the effectiveness of the UA-lowering therapy.

Typically, UA-lowering therapy encompasses the use of one or a combination of these drugs: allopurinol, febuxostat, pegloticase, probenecid and probenecid with colchicine. Xanthine oxidase inhibitors —such as allopurinol or febuxostat—are the initial drugs of choice for UA-lowering therapy. See the chart for specific dosage recommendations, possible side effects and tips for these drugs.

For some patients, monotherapy with a xanthine oxidase inhibitor alone will not be enough to achieve a healthy UA level of 6.0 mg/dL. In these difficult-to-treat cases, the uricase-containing biologic, pegloticase, can dramatically lessen the uric acid burden in 6 to 8 months especially when combined with methotrexate.

Most patients must remain on UA-lowering therapy for the rest of their lives to prevent further destruction and continued pain. It is important to monitor UA level year-after-year, even after a diagnosis is made and UA-lowering therapy has achieved the target level.

Therapies to Relieve Pain and Reduce Swelling of Acute Gout

Name	Dosage	Special Instructions	Possible Side Effects	Be Aware
Allopurinol Lopurin®, Zyloprim®	100 to 800 mg per day in a single dose. The dose is started and adjusted by 100 mg every two to four weeks to achieve serum uric acid level < 6.0mg/dL. Patients with severe renal impairment should be started with an initial dose of 50 mg/day with slower dose escalation to achieve target.	Stop taking medication at the first sign of a rash, which may indicate an allergic or hypersensitivity reaction. May need to give as BID in doses over 300 mg/day to avoid nausea.	Rash, hives or itching; nausea; transaminase elevation; rare severe cutaneous reactions occur in approximately 1 in 1,000 patients.	**Minimize flares by prescribing colchicine or NSAIDs at the time of initiating treatment and until goal of a uric acid level of ≤ 6.0mg/dL is reached.** Caution with azothioprine, 6-mercaptopurine and theophylline. The risk for allopurinol hypersensitivity should be evaluated in Asian and African-American patients by checking for HLA-B58*01
Febuxostat Uloric®	40 mg per day initially then increase to 80 mg per day in two weeks if serum uric acid level not lower than 6.0 mg/dL.	Take any time of day without regard to food or antacid use.	Elevated liver enzymes (liver irritation); nausea; joint pain; rash; a new black box warning to use febuxostat cautiously in patients with known CVD or at high risk for CVD.	**Minimize flares by prescribing colchicine or NSAIDs at the time of initiating treatment and until goal of a uric acid level of ≤ 6.0mg/dL is reached.** Contraindicated with azothioprine, 6-mercaptopurine and theophylline. New black box warning to use febuxostat cautiously in patients with known CVD or at high risk for CVD.
Pegloticase Krystexxa®	8 mg given via IV every 2 weeks	For use in difficult to control hyperuricemia and advanced gout.	Infusion reactions are greatly reduced, and efficacy improved when given concomitantly with methotrexate.	This drug should be given in a monitored infusion center. Check for G6PD deficiency prior to starting.
Probenecid Benemid®, Probalan®	500 to 3,000 mg per day in two or three divided doses.	Take with food or an antacid. Drink plenty of fluids. Do not take with aspirin or other NSAIDs. Avoid alcohol.	Headache; loss of appetite; nausea or vomiting.	Ineffective in patients with GFR less than 50. Should not be used with history of kidney stones.
Probenecid and colchicine Col-Benemid®, Col-Probenecid®, Proben-C®	One tablet (contains 500 mg probenecid and 0.5 mg colchicine) twice per day.	Take with food or an antacid. Drink plenty of fluids. Do not take with aspirin or other NSAIDs. Avoid alcohol.	Diarrhea; headache; loss of appetite; nausea or vomiting; stomach pain; rash.	Ineffective in patients with GFR less than 50. Should not be used with history of kidney stones.

Diet and Lifestyle Tips

The ACR Guidelines on gout management include lifestyle changes as well as the non-pharmacologic approach for patients to follow. General health recommendations from the ACR are weight loss—especially for patients who are obese—exercise and an overall healthy diet that eliminates certain foods that are particularly high in purines or are very likely to elevate UA levels.

Specifically, patients should avoid organ meats (liver, kidneys and tongue) and beverages sweetened with high-fructose corn syrup. Alcohol overuse—which for men is more than two alcoholic drinks per day and for women is more than one drink per day—should also be discouraged. In addition, there are several foods that should be limited, including red meat such as beef, lamb or pork, and shellfish. The guidelines encourage the use of non-fat or low-fat dairy products. Dairy products not only provide a good source of protein, especially the non-fat or low-fat varieties, but also contain casein, which can help lower UA.

Patients should also stop tobacco use, if applicable, and stay well-hydrated.

It's also worth noting that, while diet can play a role in gout management, it is often over-prioritized by many gout patients. In fact, half of those with gout say that making changes to their diet is the first step they take to manage the disease—even ahead of taking medications to lower their uric acid levels and maintaining an overall healthy fitness level. Three in four with gout incorrectly believe that they can avoid taking daily medications if they follow a healthy diet. While those with gout are encouraged to follow a healthy and balanced diet, effective gout management also includes talking to your patients about taking steps to lower their UA levels to 6.0 mg/dL or below and making other healthy lifestyle changes.

Barriers to Treatment

The most pervasive barrier standing between the proper management of gout arguably remains the ability of healthcare providers to correctly diagnose and appropriately treat the disease, and their success convincing patients to embrace a treatment regimen for life.

Also, distrust in the healthcare system and a propensity to bypass traditional therapies in favor of natural remedies can deter proper treatment among certain populations. Medical folklore is another issue; the mythology surrounding gout, patient profiles and treatment must be overcome.

The result of healthcare disparities in rural areas and other countries have contributed to increased prevalence in certain populations. This limits access to therapies, especially newer therapies, making it more difficult for patients to see a doctor and receive treatment.

Tips for All Patients

Clinicians should make sure gout patients understand the following:

1. Gout develops due to an accumulation of UA over time in the form of monosodium urate crystals. By the time patients experience symptoms and see a doctor, accumulation of excess uric acid in their bodies has been going on for years—or even decades. Even if they begin UA-lowering therapy and achieve the appropriate target serum uric acid, it can take several years to reduce the body's burden of uric acid to a point where flares no longer occur.

2. Patients with gout should check their uric acid levels every six months and aim for a healthy level of 6.0 mg/dL or below. If they already have evidence of tophi, then this target level should be 5.0 mg/dL, or even below 4.0 mg/^dL. If their UA level is not within these targets, patients need to discuss the reason with their healthcare provider. Patients are not going to improve until they achieve the target level.

3. After initiating UA-lowering therapy, there may be a period of three to six months when patients could potentially have an increased frequency of flares, unless the clinician ensures that the patient is on prophylactic anti-inflammatory therapies. Multiple gout treatment guidelines have recommended beginning either daily low-dose colchicine or low- dose NSAIDs two weeks prior to the initiation of any UA-lowering therapy. Caution patients that even though flares may become more frequent during the effort to lower their UA level, it is critical to stay on the treatment.

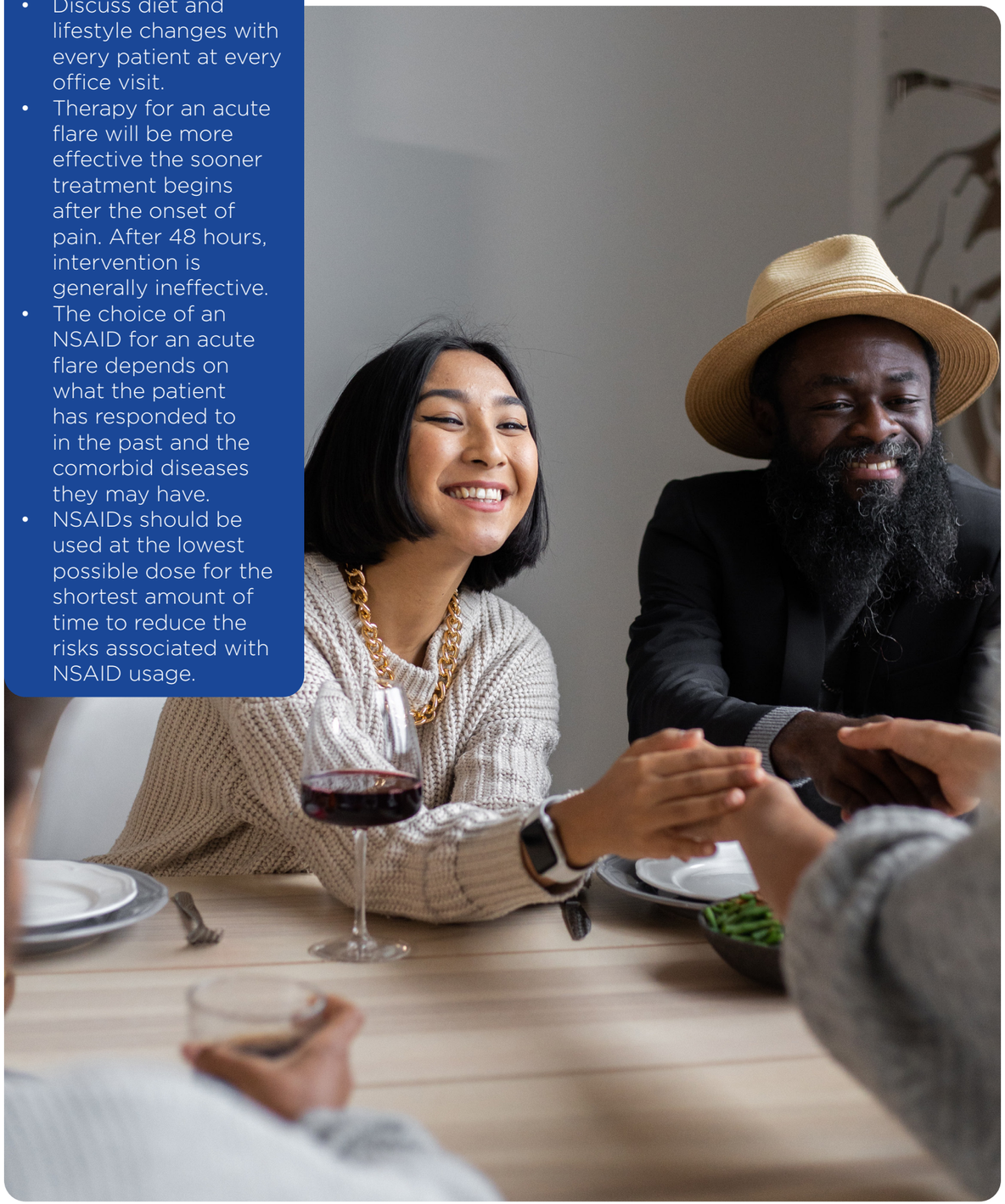
4. Patients with gout should always have a supply of their anti-inflammatory medication (NSAIDs, colchicine or prednisone) immediately available to them so that, at the earliest signs of a gout flare, they can begin treatment.

5. Heat tends to worsen symptoms. Research suggests that using ice on the affected joints helps to decrease the pain for some patients. Immobilizing the joint can help to minimize pain as well.

6.Frequent monitoring of UA level is important when initiating UA-lowering therapy and during the medication adjustment period. Once at their personal target, patients should have their UA level tested every six months. This is important because changes in diet, medications or other diseases could cause a fluctuation in UA level.

7. All patients with gout should be encouraged to maintain healthy lifestyles including exercise, weight reduction (where appropriate) and sticking to a heart-friendly diet, such as the DASH or Mediterranean diet. Avoiding fructose-sweetened beverages is also important.

- Discuss diet and lifestyle changes with every patient at every office visit.
- Therapy for an acute flare will be more effective the sooner treatment begins after the onset of pain. After 48 hours, intervention is generally ineffective.
- The choice of an NSAID for an acute flare depends on what the patient has responded to in the past and the comorbid diseases they may have.
- NSAIDs should be used at the lowest possible dose for the shortest amount of time to reduce the risks associated with NSAID usage.



Gout and Comorbid Conditions

Gout is closely linked to a number of other serious health conditions. This makes prompt diagnosis of gout and ongoing management of comorbidities important. The most common comorbid diseases are coronary artery disease, hypertension, type 2 diabetes, chronic kidney disease, hyperlipidemia and metabolic syndrome. All are associated with obesity and elevated UA levels. In fact, an obese patient is four times more likely to develop gout than someone with a normal body weight.

Encourage your patients to know—and keep track of—their healthy benchmark numbers, like uric acid, blood pressure, heart rate, cholesterol and blood sugar.

Heart Disease

Studies have shown a strong correlation between gouty arthritis and cardiovascular issues—including high blood pressure, blocked arteries and heart failure. Those who suffer from gout are more likely to have unhealthy cholesterol and lipid levels and, conversely, those who have high lipid levels and high triglycerides are more likely to develop gout.

There are also several serious heart-related complications associated with hyperuricemia, including an increased risk for acute myocardial infarction (MI)—with gout patients approximately **twice as likely** to experience a heart attack or stroke compared with those who do not have gout. Additionally, hyperuricemia has been found to increase a patient's risk of experiencing coronary artery disease or cerebrovascular disease. Those with hyperuricemia are also at an increased risk for cardiovascular mortality.

While gout and heart health issues can affect anyone, women with gout are **3.5 times more likely** to have a heart attack than men and **10 times more likely** than women without gout.

Diabetes

While more research is needed, studies have shown a strong correlation between gouty arthritis and diabetes. Those who have gout and hyperuricemia have been found to be at an increased risk for type 2 diabetes. At the same time, those who already have type 2 diabetes are more likely to have hyperuricemia, which can lead to painful gout flares.

Studies have also shown that insulin resistance may play a role in developing gout and that hyperuricemia may worsen insulin resistance. Insulin resistance has also been associated with obesity and high blood pressure, which are risk factors for gout.

While anyone with gout can develop diabetes, risk is especially high among women—with recent studies showing that women who have gout are **71%** more likely to develop diabetes than women who do not have gout.

Kidney Disease

Those who have gout are more likely to develop renal disease—and likewise, those who have renal disease are more likely to suffer from gout and hyperuricemia. For those who have renal disease, it will be more difficult for their kidneys to eliminate uric acid.

Over time, elevated uric acid levels can lead to painful gout flares and decreased renal function. Hyperuricemia can lead to tissue deposition of monosodium urate crystals (MSU). Uric acid stones—a common cause of radiolucent kidney stones—can also develop. Research has shown that **one in five people with gout will develop kidney stones**. Left untreated, these stones can block the urinary tract and result in infection, or even chronic kidney disease and loss of kidney function.

Hyperuricemia can also lead to interstitial nephropathy, in which the spaces between the kidney tubules become inflamed and can interfere with kidney function. Interstitial nephropathy can either be acute or chronic—and can eventually result in kidney failure.

Gout & Bone and Joint Health

Subcutaneous tophi—or a buildup of monosodium urate crystals—can develop in fibrous tissue around the joints as a result of gout. Even in the early-stages of gout—before the patient develops symptoms—urate crystals begin depositing in and around the joints. This is characterized by a thin layer of crystals across the cartilage in the joint, or small nodules of crystals deposited inside the joint. The nodules grow over time and can be felt on physical examination. These nodules can become large and disfiguring and their presence adjacent to bone and cartilage can directly cause tissue destruction.

The point at which a deformity begins will vary significantly from person to person. The higher the serum UA level, the more rapidly tophi deposits will accumulate around the joints and lead to damage. Timely and ongoing treatment is needed to reduce long-term and permanent bone, joint and tissue damage.

Ethnicity and Comorbidities

The incidence of comorbid conditions that can impact gout also varies by ethnicity. For instance, obesity is a particular problem in both Hispanic and African-American populations. African Americans are also more likely to develop hypertension, while Hispanics are more likely to develop type 2 diabetes.

- Gout patients frequently have serious comorbid conditions, requiring a comprehensive approach to treatment.
- Regular monitoring of UA level is especially important for patients with comorbidities.
- Some medications prescribed for comorbidities can increase UA levels and an alternative may be needed.

Medications and Comorbidities

Managing medications for patients with comorbid diseases requires ongoing vigilance. Some of the more common treatments can increase UA levels and adversely affect gout. For example, treating patients who have high cholesterol with niacin to lower triglycerides can increase UA levels.

Encourage these patients to gain control of their diet and use fenofibrate, which helps lower UA, instead of niacin. Some hypertension medicines, such as HCTZ, can also significantly elevate UA levels. They can cause more frequent flares or make it more difficult to control UA levels. Switching to a different blood pressure medication may help resolve this problem.

To access free information and resources about gout for you and your patients, visit **GoutEducation.org**.

Further Reading: **Seminal Research Studies on Gout Diagnosis and Management**

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